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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,445	07/23/2003	Timothy Lovenberg	JJPR-0032	1837

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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,445	LOVENBERG ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6, 16* is/are allowed.

6)☒ Claim(s) *1-3, 5, 8, 11-12* is/are rejected.

7)☒ Claim(s) *4, 7, 9, 10, 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 – 13 and 16 are pending and under examination in this Office action.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings are objected to because Figures 1 and 2 do not contain the appropriate SEQ ID NO. The SEQ ID NO should appear on either the drawing itself or in the Brief Description of the Drawings in the Specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

1) The first paragraph of the amendment filed Jul 23, 2003 claims priority from application 09/790849. Although the application was pending at the time the instant application was filed, it has since been abandoned and the text should be changed to indicate this.

2) On page 11, the protein is reported to have a molecular weight of 44,495 kDa. This is probably an error; Applicants probably meant that the molecular weight is 44,495 Daltons.

3) The examples are not sequentially numbered. The specification skips from Example 1 to Example 4, although it appears that no pages are missing.

4) Page 39 of the specification refers to a PCR-generated sequence, depicted in Figure 6. However Figure 6 is an amino acid sequence, which could not be directly generated by PCR.

5) The correct title of the second reference cited by Applicant on page 53 is "Guanine nucleotides and pertussis toxin reduce the affinity of histamine H3 receptors on AtT-20 cells."

Appropriate correction is required.

Claim Objections

Claims 4, 7, 9, 10, and 13 are objected to because of the following informalities: they use indefinite articles to refer to unique sequences. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 – 3, 5, and 12 rejected under 35 U.S.C. 102(e) as being anticipated by Behan et al. (US Patent 6,204,017 issue date March 20, 2001, filing date October 7, 1999). The claims are directed towards at least 15 consecutive nucleotides encoding a mammalian histamine H4 receptor. Nucleotides numbered 132 – 151 of SEQ ID NO: 5 from the present application match perfectly with the same nucleotides of SEQ ID NO: 1 of Behan et al., which Behan et al. disclose is a novel human G-protein-coupled receptor that binds histamine. The nucleotide

sequence disclosed by Behan et al. is 58.4% identical to SEQ ID NO: 5 of the present application and at the amino acid level, the polypeptide disclosed by Behan et al. (their SEQ ID NO: 2), is 66.9% identical to SEQ ID NO: 8 of the instant application. Behan et al. teach the use of either a DNA or RNA molecule (column 7, lines 2 and 3). Thus the nucleotide sequence disclosed by Behan et al. meets all the limitations of claim 1(c). Accordingly, claim 1 is rejected under 35 U.S.C. 102 (e), as are claims 2, 3, 5, and 12, which depend from the same interpretation of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 3, 5, and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 1(b) is drawn to a nucleic acid molecule that is complementary to a nucleic acid molecule that encodes a histamine H4 receptor. However, if sequence X encodes polypeptide Y, the complement of X will not encode polypeptide Y. The nucleic acid of claim 1(b) does not encode a histamine H4 receptor, and the specification does not teach how to use a polypeptide encoded by polynucleotides that are complementary to an H4-encoding sequence. Claim 1(d) is drawn to a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide sequence of claim 1(a), where stringent conditions are defined by Applicant as allowing hybridization when the sequences are 95% identical (Specification, p. 22). However, a molecule that will hybridize to a polynucleotide encoding a histamine H4 receptor will not itself encode a histamine H4 receptor, but will be complementary to it or to a polynucleotide that is 95% identical. The specification does not teach how to use a polypeptide encoded by the polynucleotides of claims 1(b) and 1(d). Claim 1 is therefore rejected, as are claims 2, 3, 5, and 12, which depend from the same interpretations of claim 1.

Claims 1 – 3, 5, and 12 are also rejected under 35 U.S.C. 112, first paragraph, for failing to provide a complete written description of the invention. Claim 1(c) is drawn to isolated polynucleotides encoding mammalian histamine H4 receptors that comprise at least 15 consecutive nucleotides that encode SEQ ID NO: 8. However, there is no guidance in the specification as to which 15 nucleotides should be used, nor is there a written description of what such a histamine receptor may look like, how it might bind histamine, or how it might signal. Thus the specification fails to provide an adequate written description of the invention claimed in claim 1 (c). Claim 1 is therefore rejected, as are claims 2, 3, 5, and 12, which depend from the same interpretation of claim 1.

Since the instant disclosure does not give sufficient guidance as to how to make and use specific instances of the invention, the genus claims cannot be allowed, as the claimed genera encompass a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a polynucleotide or polypeptide, such as *either* the polynucleotides that contain at least 15 consecutive nucleotides encoding SEQ ID NO: 8, as in claim 1 (c) or polynucleotides that are at least 95% identical to polynucleotides encoding SEQ ID NO: 8, as in claim 1 (d) "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement

that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of DNAs may be achieved by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses four polypeptide sequences for receptors and four polynucleotide sequences encoding them, but does not indicate which regions are crucial for the proper folding or biological activity of the mature receptor. Furthermore, receptor function cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does not allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences.

Claims 5, 8, and 11 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to isolated genomic DNA molecules encoding histamine H4 receptors. While specific cDNA sequences encoding said receptors are disclosed by Applicant, no genomic DNA sequences have been disclosed. There is no description of the size of the genomic locus encoding the protein, nor is there even a mention of the numbers of introns and exons contained within the genomic sequence, let alone a complete disclosure of the genomic sequence. There are no well-established rules,

techniques, or procedures that would allow one of ordinary skill in the art to determine the genomic sequence given the disclosed cDNA sequences, thus the claims to genomic DNAs do not meet the written description requirement.

Conclusion

Claims 1 – 3, 5, 8, and 11 – 12 are rejected. Claims 4, 7, 9, 10, and 13 are objected to. Claims 6 and 16 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 9:00AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eileen B O'Hara

Daniel E. Kolker, Ph.D.

EILEEN B. O'HARA
PATENT EXAMINER